Page No.:

- (11)  $-(CH_2)_nCOR^8$ ,
- (12)  $-(CH_2)_nNR^8C(O)R^8$ ,
- (13)  $-(CH_2)_nNR^8CO_2R^8$ ,
- (14)  $-(CH_2)_nNR^8C(O)N(R^8)_2$ ,
- (15)  $-(CH_2)_nNR^8SO_2R^8$ ,
- (16)  $-(CH_2)_nS(O)_pR^8$ ,
- (17)  $-(CH_2)_nSO_2N(R^8)_2$ ,
- (18)  $-(CH_2)_nOR^8$ ,
- (19)  $-(CH_2)_nOC(O)R^8$ ,
- (20)  $-(CH_2)_nOC(O)OR^8$ ,
- (21)  $-(CH_2)_nOC(O)N(R^8)_2$ ,
- (22)  $-(CH_2)_nN(R^8)_2$ , and
- (23)  $-(CH_2)_nNR^8SO_2N(R^8)_2$ ,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl;

R<sup>1</sup> is selected from the group consisting of

- (1) hydrogen,
- (2) amidino,
- (3) C<sub>1-4</sub> alkyliminoyl,
- (4)  $C_{1-10}$  alkyl,
- (5)  $-(CH_2)_n$ -C<sub>3-7</sub> cycloalkyl,
- (6)  $-(CH_2)_n$ -phenyl,
- (7)  $-(CH_2)_n$ -naphthyl, and
- (8) -(CH<sub>2</sub>)<sub>n</sub>-heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and oxo;

R<sup>2</sup> is selected from the group consisting of

(1) phenyl,

Page No.: 4

- (2) naphthyl, and
- (3) heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>;

each R<sup>3</sup> is independently selected from the group consisting of

- (1)  $C_{1-8}$  alkyl,
- (2) C<sub>2-8</sub> alkenyl,
- (3)  $-(CH_2)_n$ -phenyl,
- (4)  $-(CH_2)_n$ -naphthyl,
- (5)  $-(CH_2)_n$ -heteroaryl,
- (6)  $-(CH_2)_nC_2-7$  heterocycloalkyl,
- (7)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (8) halogen,
- (9)  $OR^9$ ,
- (10)  $-(CH_2)_nC(O)R^9$ ,
- (11)  $-(CH_2)_nOC(O)R^9$ ,
- (12)  $-(CH_2)_nC(O)OR^9$ ,
- (13)  $-(CH_2)_nC\equiv N$ ,
- (14) NO<sub>2</sub>,
- (15)  $-(CH_2)_nN(R^9)_2$ ,
- (16)  $-(CH_2)_nC(O)N(R^9)_2$ ,
- (17)  $-(CH_2)_nNR^9C(O)R^9$ ,
- (18)  $-(CH_2)_nNR^9C(O)OR^9$ ,
- (19)  $-(CH_2)_nNR^9C(O)$ -heteroaryl,
- (20)  $-(CH_2)_nNR^9C(O)N(R^9)_2$ ,
- (21)  $-(CH_2)_nC(O)NR^9N(R^9)_2$ ,
- (22)  $-(CH_2)_nC(O)NR^9NR^9C(O)R^9$ ,
- (23)  $-(CH_2)_nNR^9S(O)_pR^9$ ,
- (24)  $-(CH_2)_nS(O)_pN(R^9)_2$ ,
- (25)  $-(CH_2)_nS(O)_pR^9$ ,
- (26)  $O(CH_2)_nC(O)N(R^9)_2$ ,
- (27) CF<sub>3</sub>,
- (28) CH<sub>2</sub>CF<sub>3</sub>,

Page No.: 5

- (29) OCF3, and
- (30) OCH<sub>2</sub>CF<sub>3</sub>,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH<sub>2</sub>) carbon atom in  $R^3$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, oxo,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, or two  $R^3$  substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each R4 is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3)  $-(CH_2)_nC_{3-6}$  cycloalkyl,
- (4)  $-(CH_2)_n$ -aryl,
- (5) hydroxy,
- (6) halogen, and
- (7) amino;

R<sup>5</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3)  $C_{2-8}$  alkenyl,
- (4) C<sub>2-8</sub> alkynyl,
- (5)  $C_{1-8}$  alkoxy,
- (6)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (7)  $-(CH_2)_nC_2-7$  heterocycloalkyl,
- (8)  $-(CH_2)_n$ -phenyl,
- (9)  $-(CH_2)_n$ -naphthyl,
- (10)  $-(CH_2)_n$ -heteroaryl, and
- (11)  $-(CH_2)_nC_3-7$  bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and

Serial No.:

10/788,859 21291Y

Case No.: Page No.:

6

oxo, and wherein any methylene (CH<sub>2</sub>) in R<sup>5</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1-4</sub> alkyl;

R6 is selected from the group consisting of

- (1) hydrogen, and
- (2)  $C_{1-8}$  alkyl;

R<sup>7</sup> is selected from the group consisting of

- (1)  $-(CH_2)_nN(R^8)_2$ ,
- (2)  $-(CH_2)_nNR^8C(O)R^8$ ,
- (3)  $-(CH_2)_nNR^8C(O)OR^8$ ,
- (4)  $-(CH_2)_nNR^8C(O)N(R^8)_2$ ,
- (5)  $-(CH_2)_nNR^8S(O)R^8$ ,
- (6)  $-(CH_2)_nNR^8S(O)_2R^8$ , and
- (7)  $-(CH_2)_nNR^8S(O)_2N(R^8)_2$ ,

wherein any methylene (CH<sub>2</sub>) in  $R^7$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl, or two  $R^8$  substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from  $C_{1-8}$  alkyl and oxo;

each R8 is independently selected from the group consisting of

- (1) hydrogen,
- (2) C<sub>1-8</sub> alkyl,
- (3)  $C_{2-8}$  alkenyl,
- (4)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (5) -(CH<sub>2</sub>)<sub>n</sub>C<sub>2</sub>-7 heterocycloalkyl,
- (6) -(CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-7 bicycloalkyl,
- (7)  $-(CH_2)_n$ -phenyl,
- (8)  $-(CH_2)_n$ -naphthyl, and
- (9)  $-(CH_2)_n$ -heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and

Page No.: 7

wherein any methylene (CH<sub>2</sub>) in  $R^8$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl, or two  $R^8$  groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

each R<sup>9</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) -(CH<sub>2</sub>)<sub>n</sub> heterocycloalkyl, and
- (6) C<sub>3</sub>-6 cycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C<sub>1-4</sub> alkyl, hydroxy, and C<sub>1-4</sub> alkoxy, or two R<sup>9</sup> groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

```
r is 1 or 2;
s is 0, 1, or 2;
m is 0, 1, 2, 3, or 4;
n is 0, 1, 2, 3, or 4; and
p is 0, 1, or 2.
```

- 2. (original) The compound of Claim 1 wherein R<sup>1</sup> is selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyl, -(CH<sub>2</sub>)<sub>0-1</sub>C<sub>3-6</sub> cycloalkyl, and -(CH<sub>2</sub>)<sub>0-1</sub>-phenyl, wherein phenyl is unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and alkyl and cycloalkyl are optionally substituted with one to three groups independently selected from R<sup>3</sup> and oxo; and pharmaceutically acceptable salts thereof.
- 3. (original) The compound of Claim 1 wherein R<sup>2</sup> is phenyl or thienyl, optionally substituted with one to three groups independently selected from R<sup>3</sup>; and pharmaceutically acceptable salts thereof.
  - 4. (original) The compound of Claim 3 wherein  $\mathbb{R}^2$  is phenyl optionally

Page No.: 8

substituted with one to three groups independently selected from R<sup>3</sup>; and pharmaceutically acceptable salts thereof.

5. (original) The compound of Claim 1 wherein each R<sup>4</sup> is independently selected from the group consisting of hydrogen, halogen, or hydroxy; and pharmaceutically acceptable salts thereof.

6. (original) The compound of Claim 1 wherein X is selected from the group consisting of

- (1)  $C_{1-8}$  alkyl,
- (2)  $-(CH_2)_nC_3-8$  cycloalkyl,
- (3)  $-(CH_2)_n$ -phenyl,
- (4)  $-(CH_2)_n$ -heteroaryl,
- (5) -(CH<sub>2</sub>)<sub>n</sub>heterocycloalkyl, and
- (6)  $-(CH_2)_nC(R^5)(R^6)(R^7)$ ,

wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl; and pharmaceutically acceptable salts thereof.

- 7. (original) The compound of Claim 6 wherein X is phenyl or heteroaryl optionally substituted with one to three groups independently selected from R<sup>3</sup>; and pharmaceutically acceptable salts thereof.
- 8. (original) The compound of Claim 7 wherein X is phenyl optionally substituted with one to three groups independently selected from R<sup>3</sup>; and pharmaceutically acceptable salts thereof.
- 9. (original) The compound of Claim 6 wherein X is  $-(CH_2)_nC(R^5)(R^6)(R^7)$ ; and pharmaceutically acceptable salts thereof.
  - 10. (original) The compound of Claim 9 wherein

n is 0;

R<sup>5</sup> is selected from the group consisting of

Page No.: 9

(1) C<sub>1-8</sub> alkyl,

(2)  $-(CH_2)_nC_3-7$  cycloalkyl,

(3) -(CH<sub>2</sub>)<sub>n</sub>C<sub>2</sub>-7 heterocycloalkyl,

(4)  $-(CH_2)_n$ -phenyl, and

(5)  $-(CH_2)_n$ -heteroaryl,

wherein phenyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, cycloalkyl and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in  $R^5$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl; and

R<sup>6</sup> is hydrogen; and pharmaceutically acceptable salts thereof.

- 11. (original) The compound of Claim 1 wherein r is 1.
- 12. (original) The compound of Claim 1 wherein r is 2.
- 13. (original) The compound of Claim 1 wherein R<sup>2</sup> is phenyl substituted with one to three groups independently selected from R<sup>3</sup>.
- 14. (original) The compound of Claim 1 of structural formula IIa or IIb of the indicated *trans* relative stereochemical configuration:

or a pharmaceutically acceptable salt thereof; wherein

X is selected from the group consisting of

(1)  $C_{1-8}$  alkyl,

- (2)  $-(CH_2)_nC_3-8$  cycloalkyl,
- (3)  $-(CH_2)_n$ -phenyl,

41

- (4)  $-(CH_2)_n$ -heteroaryl,
- (5) -(CH<sub>2</sub>)<sub>n</sub>heterocycloalkyl, and
- (6)  $-(CH_2)_nC(R^5)(R^6)(R^7)$ ,

wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl;

R<sup>1</sup> is selected from the group consisting of hydrogen, amidino, C<sub>1-4</sub> alkyliminoyl, C<sub>1-6</sub> alkyl, C<sub>5-6</sub> cycloalkyl, -(CH<sub>2</sub>)<sub>0-1</sub> phenyl, and -(CH<sub>2</sub>)<sub>0-1</sub> heteroaryl, wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and oxo;

R<sup>2</sup> is phenyl or thienyl, optionally substituted with one to three groups independently selected from R<sup>3</sup>;

each R<sup>3</sup> is independently selected from the group consisting of

- (1)  $C_{1-8}$  alkyl,
- (2)  $C_{2-8}$  alkenyl,
- (3)  $-(CH_2)_n$ -phenyl,
- (4)  $-(CH_2)_n$ -naphthyl,
- (5)  $-(CH_2)_n$ -heteroaryl,
- (6) -(CH<sub>2</sub>)<sub>n</sub>C<sub>2</sub>-7 heterocycloalkyl,
- (7)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (8) halogen,
- (9)  $OR^9$ ,
- (10)  $-(CH_2)_nC(O)R^9$ ,
- (11)  $-(CH_2)_nOC(O)R^9$ ,
- (12)  $-(CH_2)_nC(O)OR^9$ ,
- (13) -(CH<sub>2</sub>)<sub>n</sub>C≡N,
- (14) NO<sub>2</sub>,
- (15)  $-(CH_2)_nN(R^9)_2$ ,
- (16)  $-(CH_2)_nC(O)N(R^9)_2$ ,

- (17)  $-(CH_2)_nNR^9C(O)R^9$ ,
- (18)  $-(CH_2)_nNR^9C(O)OR^9$ ,
- (19) -(CH<sub>2</sub>)<sub>n</sub>NR<sup>9</sup>C(O)-heteroaryl,
- (20)  $-(CH_2)_nNR^9C(O)N(R^9)_2$ ,
- (21)  $-(CH_2)_nC(O)NR^9N(R^9)_2$ ,
- (22)  $-(CH_2)_nC(O)NR^9NR^9C(O)R^9$ ,
- (23)  $-(CH_2)_nNR^9S(O)_pR^9$ ,
- (24)  $-(CH_2)_nS(O)_pN(R^9)_2$ ,
- (25)  $-(CH_2)_nS(O)_pR^9$ ,
- (26)  $O(CH_2)_nC(O)N(R^9)_2$ ,
- (27) CF<sub>3</sub>,
- (28) CH<sub>2</sub>CF<sub>3</sub>,
- (29) OCF3, and
- (30) OCH<sub>2</sub>CF<sub>3</sub>,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH<sub>2</sub>) carbon atom in  $R^3$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, oxo,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, or two  $R^3$  substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each R4 is independently selected from the group consisting of

- (1) hydrogen,
- (2) C<sub>1-8</sub> alkyl,
- (3) -(CH<sub>2</sub>)<sub>0-1</sub>C<sub>3-6</sub> cycloalkyl,
- (4)  $-(CH_2)_{0-1}$ -aryl,
- (5) hydroxy,
- (6) halogen, and
- (7) amino;

R<sup>5</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2) C<sub>1-8</sub> alkyl,
- (3) C<sub>2-8</sub> alkenyl,

- (4) C<sub>2-8</sub> alkynyl,
- (5)  $C_{1-8}$  alkoxy,
- (6)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (7) -(CH<sub>2</sub>)<sub>n</sub>C<sub>2</sub>-7 heterocycloalkyl,
- (8)  $-(CH_2)_n$ -phenyl,
- (9)  $-(CH_2)_n$ -naphthyl,
- (10) -(CH<sub>2</sub>)<sub>n</sub>-heteroaryl, and
- (11) -(CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-7 bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, alkenyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in  $R^5$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl;

R6 is selected from the group consisting of

- (1) hydrogen, and
- (2)  $C_{1-8}$  alkyl;

R<sup>7</sup> is selected from the group consisting of

- (1)  $-(CH_2)_nN(R^8)_2$ ,
- (2)  $-(CH_2)_nNR^8C(O)R^8$ ,
- (3)  $-(CH_2)_nNR^8C(O)OR^8$ ,
- (4)  $-(CH_2)_nNR^8C(O)N(R^8)_2$ ,
- (5)  $-(CH_2)_nNR^8S(O)R^8$ ,
- (6)  $-(CH_2)_nNR^8S(O)_2R^8$ , and
- (7)  $-(CH_2)_nNR^8S(O)_2N(R^8)_2$ ,

wherein any methylene (CH<sub>2</sub>) in  $R^7$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl, or two  $R^8$  substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from  $C_{1-8}$  alkyl and oxo;

each R8 is independently selected from the group consisting of

(1) hydrogen,

- (2)  $C_{1-8}$  alkyl,
- (3)  $C_{2-8}$  alkenyl,
- (4)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (5) -(CH<sub>2</sub>)<sub>n</sub>C<sub>2</sub>-7 heterocycloalkyl,
- (6) -(CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-7 bicycloalkyl,
- (7)  $-(CH_2)_n$ -phenyl,
- (8) -(CH<sub>2</sub>)<sub>n</sub>-naphthyl, and
- (9) -(CH<sub>2</sub>)<sub>n</sub>-heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and wherein any methylene (CH<sub>2</sub>) in R<sup>8</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1-4</sub> alkyl, or two R<sup>8</sup> groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

each R<sup>9</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) -(CH<sub>2</sub>)<sub>n</sub> heterocycloalkyl, and
- (6) C3-6 cycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C<sub>1-4</sub> alkyl, hydroxy, and C<sub>1-4</sub> alkoxy, or two R<sup>9</sup> groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

```
r is 1 or 2;
s is 0, 1 or 2;
m is 0, 1, 2, 3 or 4;
n is 0, 1, 2, 3 or 4; and
p is 0, 1, or 2.
```

15. (original) The compound of Claim 1 of the following structural formula with the indicated *trans* relative stereochemical configuration:

$$X-N$$
 $R^4$ 
 $R^4$ 
 $R^4$ 
 $R^5$ 
 $R^3$ 
 $R^3$ 
 $R^3$ 

or a pharmaceutically acceptable salt thereof; wherein

X is selected from the group consisting of

- (1)  $-(CH_2)_{0-1}$ -phenyl,
- (2) -(CH<sub>2</sub>)<sub>0-1</sub>-heteroaryl, and
- (3)  $-(CH_2)_{0-1}C(R^5)(R^6)(R^7)$ ,

wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and wherein any methylene (CH<sub>2</sub>) in X is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1-4</sub> alkyl;

R1 is selected from the group consisting of hydrogen, C1-4 alkyl, and -(CH2)0-1 phenyl;

each  $R^3$  is independently selected from the group consisting of

- (1)  $C_{1-8}$  alkyl,
- (2) C<sub>2-8</sub> alkenyl,
- (3)  $-(CH_2)_{0-1}$ -phenyl,
- (4)  $-(CH_2)_{0-1}$ -naphthyl,
- (5)  $-(CH_2)_{0-1}$ -heteroaryl,
- (6) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>2-7</sub> heterocycloalkyl,
- (7)  $-(CH_2)_{0-1}-C_{3-7}$  cycloalkyl,
- (8) halogen,
- (9)  $OR^9$ ,
- (10)  $-(CH_2)_{0-1}-C(O)R^9$ ,
- (11)  $-(CH_2)_{0-1}-OC(O)R^9$ ,
- (12)  $-(CH_2)_{0-1}-C(O)OR^9$ ,
- (13)  $-(CH_2)_{0-1}-C\equiv N$ ,
- (14) NO<sub>2</sub>,

(15)  $-(CH_2)_{0-1}-N(R^9)_2$ ,

a

- (16)  $-(CH_2)_{0-1}-C(O)N(R^9)_2$ ,
- (17)  $-(CH_2)_{0-1}-NR^9C(O)R^9$ ,
- (18)  $-(CH_2)_{0-1}-NR^9C(O)OR^9$ ,
- (19) -(CH<sub>2</sub>)<sub>0-1</sub>NR<sup>9</sup>C(O)-heteroaryl,
- (20)  $-(CH_2)_{0-1}NR^9C(O)N(R^9)_2$ ,
- (21)  $-(CH_2)_{0-1}C(O)NR^9N(R^9)_2$ ,
- (22)  $-(CH_2)_{0-1}-C(O)NR^9NR^9C(O)R^9$ ,
- (23)  $-(CH_2)_{0-1}-NR^9S(O)_{1-2}R^9$ ,
- (24)  $-(CH_2)_{0-1}-S(O)_{1-2}N(R^9)_2$ ,
- (25)  $-(CH_2)_{0-1}-S(O)_{0-2}R^9$ ,
- (26)  $O(CH_2)_{0-1}-C(O)N(R^9)_2$ ,
- (27) CF<sub>3</sub>,
- (28) CH<sub>2</sub>CF<sub>3</sub>,
- (29) OCF3, and
- (30) OCH<sub>2</sub>CF<sub>3</sub>,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH<sub>2</sub>) carbon atom in  $R^3$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, oxo,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, or two  $R^3$  substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each R4 is independently selected from the group consisting of

- (1) hydrogen,
- (2) C<sub>1-8</sub> alkyl,
- (3)  $-(CH_2)_{0-1}-C_{3-6}$  cycloalkyl,
- (4)  $-(CH_2)_{0-1}$ -aryl,
- (5) hydroxy,
- (6) halogen, and
- (7) amino;

R<sup>5</sup> is independently selected from the group consisting of

(1) hydrogen,

(2)  $C_{1-8}$  alkyl,

W

- (3)  $C_{2-8}$  alkenyl,
- (4)  $C_{2-8}$  alkynyl,
- (5) C<sub>1-8</sub> alkoxy,
- (6)  $-(CH_2)_{0-1}-C_{3-7}$  cycloalkyl,
- (7) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>2-7</sub> heterocycloalkyl,
- (8)  $-(CH_2)_{0-1}$ -phenyl,
- (9)  $-(CH_2)_{0-1}$ -naphthyl,
- (10)  $-(CH_2)_{0-1}$ -heteroaryl, and
- (11) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>3</sub>-7 bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, alkenyl, alkynyl, alkoxy, cycloalky, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in  $R^5$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl;

R<sup>6</sup> is selected from the group consisting of

- (1) hydrogen, and
- (2)  $C_{1-8}$  alkyl;

R<sup>7</sup> is selected from the group consisting of

- (1)  $-(CH_2)_{0-3}-N(R^8)_{2}$ ,
- (2)  $-(CH_2)_{0-3}-NR^8C(O)R^8$ ,
- (3)  $-(CH_2)_{0-3}-NR^8C(O)OR^8$ ,
- (4)  $-(CH_2)_{0-3}-NR^8C(O)N(R^8)_{2}$ ,
- (5)  $-(CH_2)_{0-3}-NR^8S(O)R^8$ ,
- (6)  $-(CH_2)_{0-3}-NR^8S(O)_2R^8$ , and
- (7)  $-(CH_2)_{0-3}-NR^8S(O)_2N(R^8)_2$ ,

wherein any methylene (CH<sub>2</sub>) in  $R^7$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl, or two  $R^8$  substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from  $C_{1-8}$  alkyl and oxo;

each R8 is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) C<sub>2-8</sub> alkenyl,
- (4)  $-(CH_2)_{0-1}-C_{3-7}$  cycloalkyl,
- (5) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>2</sub>-7 heterocycloalkyl,
- (6)  $-(CH_2)_{0-1}-C_{3-7}$  bicycloalkyl,
- (7)  $-(CH_2)_{0-1}$ -phenyl,
- (8) -(CH<sub>2</sub>)<sub>0-1</sub>-naphthyl, and
- (9)  $-(CH_2)_{0-1}$ -heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and wherein any methylene (CH<sub>2</sub>) in  $R^8$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl, or two  $R^8$  groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

each R<sup>9</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) -(CH<sub>2</sub>)<sub>0-1</sub> heterocycloalkyl, and
- (6) C<sub>3</sub>-6 cycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C<sub>1-4</sub> alkyl, hydroxy, and C<sub>1-4</sub> alkoxy, or two R<sup>9</sup> groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

- r is 1 or 2; s is 0, 1 or 2; and
- m is 0, 1, 2, 3 or 4.

16. (original) A compound of structural formula IV:

or a pharmaceutically acceptable salt thereof; wherein

R1 is selected from the group consisting of

- (1) hydrogen,
- (2) amidino,
- (3) C<sub>1-4</sub> alkyliminoyl,
- (4) C<sub>1-10</sub> alkyl,
- (5)  $-(CH_2)_n$ -C3-7 cycloalkyl,
- (6)  $-(CH_2)_n$ -phenyl,
- (7)  $-(CH_2)_n$ -naphthyl, and

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and oxo;

R<sup>2</sup> is selected from the group consisting of

- (1) phenyl,
- (2) naphthyl, and
- (3) heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>;

each R<sup>3</sup> is independently selected from the group consisting of

- (1)  $C_{1-8}$  alkyl,
- (2) C<sub>2-8</sub> alkenyl,
- (3)  $-(CH_2)_n$ -phenyl,
- (4)  $-(CH_2)_n$ -naphthyl,

- (5)  $-(CH_2)_n$ -heteroaryl,
- (6)  $-(CH_2)_nC_2-7$  heterocycloalkyl,
- (7)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (8) halogen,
- (9)  $OR^9$ ,

'n

- (10)  $-(CH_2)_nC(O)R^9$ ,
- (11)  $-(CH_2)_nOC(O)R^9$ ,
- (12)  $-(CH_2)_nC(O)OR^9$ ,
- (13) -(CH<sub>2</sub>)<sub>n</sub>C≡N,
- (14) NO<sub>2</sub>,
- (15)  $-(CH_2)_nN(R^9)_2$ ,
- (16)  $-(CH_2)_nC(O)N(R^9)_2$ ,
- (17)  $-(CH_2)_nNR^9C(O)R^9$ ,
- (18)  $-(CH_2)_nNR^9C(O)OR^9$ ,
- (19)  $-(CH_2)_nNR^9C(O)$ -heteroaryl,
- (20)  $-(CH_2)_nNR^9C(O)N(R^9)_2$ ,
- (21)  $-(CH_2)_nC(O)NR^9N(R^9)_2$ ,
- (22)  $-(CH_2)_nC(O)NR^9NR^9C(O)R^9$ ,
- (23)  $-(CH_2)_nNR^9S(O)_pR^9$ ,
- (24)  $-(CH_2)_nS(O)_pN(R^9)_2$ ,
- (25)  $-(CH_2)_nS(O)_pR^9$ ,
- (26)  $O(CH_2)_nC(O)N(R^9)_2$ ,
- (27) CF<sub>3</sub>,
- (28) CH<sub>2</sub>CF<sub>3</sub>,
- (29) OCF<sub>3</sub>, and
- (30) OCH<sub>2</sub>CF<sub>3</sub>,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH<sub>2</sub>) carbon atom in  $R^3$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, oxo,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, or two  $R^3$  substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each R<sup>4</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3)  $-(CH_2)_nC_{3-6}$  cycloalkyl,
- (4)  $-(CH_2)_n$ -aryl,
- (5) hydroxy,
- (6) halogen, and
- (7) amino;

R<sup>5</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2) C<sub>1-8</sub> alkyl,
- (3) C<sub>2-8</sub> alkenyl,
- (4) C<sub>2-8</sub> alkynyl,
- (5) C<sub>1-8</sub> alkoxy,
- (6)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (7)  $-(CH_2)_nC_2-7$  heterocycloalkyl,
- (8)  $-(CH_2)_n$ -phenyl,
- (9)  $-(CH_2)_n$ -naphthyl,
- (10) -(CH<sub>2</sub>)<sub>n</sub>-heteroaryl, and
- (11) -(CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-7 bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in  $R^5$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl;

R6 is selected from the group consisting of

- (1) hydrogen, and
- (2) C<sub>1-8</sub> alkyl;

R<sup>7</sup> is selected from the group consisting of

- (1)  $-(CH_2)_nN(R^8)_2$ ,
- (2)  $-(CH_2)_nNR^8C(O)R^8$ ,
- (3)  $-(CH_2)_nNR^8C(O)OR^8$ ,

- (4)  $-(CH_2)_nNR^8C(O)N(R^8)_2$ ,
- (5)  $-(CH_2)_nNR^8S(O)R^8$ ,
- (6)  $-(CH_2)_nNR^8S(O)_2R^8$ , and
- (7)  $-(CH_2)_nNR^8S(O)_2N(R^8)_2$ ,

wherein any methylene (CH<sub>2</sub>) in  $R^7$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl, or two  $R^8$  substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from  $C_{1-8}$  alkyl and oxo;

each R8 is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) C<sub>2-8</sub> alkenyl,
- (4)  $-(CH_2)_nC_3-7$  cycloalkyl,
- (5)  $-(CH_2)_nC_2$ -7 heterocycloalkyl,
- (6) -(CH<sub>2</sub>)<sub>n</sub>C<sub>3</sub>-7 bicycloalkyl,
- (7)  $-(CH_2)_n$ -phenyl,
- (8)  $-(CH_2)_n$ -naphthyl, and
- (9)  $-(CH_2)_n$ -heteroaryl,

wherein aTkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and wherein any methylene (CH<sub>2</sub>) in R<sup>8</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1-4</sub> alkyl, or two R<sup>8</sup> groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

each R<sup>9</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) -(CH<sub>2</sub>)<sub>n</sub> heterocycloalkyl, and

Page No.:

## (6) C3-6 cycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C1-4 alkyl, hydroxy, and C1-4 alkoxy, or two R<sup>9</sup> groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC1-4 alkyl;

r is 1 or 2; 0, 1 or 2; s is 0, 1, 2, 3, or 4; m is n is 0, 1, 2, 3, or 4; and 0, 1, or 2. p is

17. (original) The compound of Claim 1 of the following structural formula with the indicated trans relative stereochemical configuration:

or a pharmaceutically acceptable salt thereof; wherein

R1 is selected from the group consisting of hydrogen, C1-4 alkyl, and -(CH<sub>2</sub>)<sub>0-1</sub> phenyl;

each R<sup>3</sup> is independently selected from the group consisting of

- C<sub>1-8</sub> alkyl, (1)
- (2) C2-8 alkenyl,
- (3) -(CH2)0-1-phenyl,
- -(CH<sub>2</sub>)<sub>0-1</sub>-naphthyl, (4)
- (5) -(CH<sub>2</sub>)<sub>0-1</sub>-heteroaryl,
- -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>2</sub>-7 heterocycloalkyl, (6)
- -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>3</sub>-7 cycloalkyl, **(7)**
- (8) halogen,

Serial No.:

10/788,859

Case No.: Page No.:

21291Y 23

- (9)  $OR^9$ ,
- (10)  $-(CH_2)_{0-1}-C(O)R^9$ ,
- (11)  $-(CH_2)_{0-1}-OC(O)R^9$ ,
- (12)  $-(CH_2)_{0-1}-C(O)OR^9$ ,
- (13)  $-(CH_2)_{0-1}-C\equiv N$ ,
- (14) NO<sub>2</sub>,
- (15)  $-(CH_2)_{0-1}-N(R^9)_2$ ,
- (16)  $-(CH_2)_{0-1}-C(O)N(R^9)_2$ ,
- (17)  $-(CH_2)_{0-1}-NR^9C(O)R^9$ ,
- (18)  $-(CH_2)_{0-1}-NR^9C(O)OR^9$ ,
- (19) -(CH<sub>2</sub>)<sub>0-1</sub>NR<sup>9</sup>C(O)-heteroaryl,
- (20)  $-(CH_2)_{0-1}NR^9C(O)N(R^9)_2$ ,
- (21)  $-(CH_2)_{0-1}C(O)NR^9N(R^9)_2$ ,
- (22)  $-(CH_2)_{0-1}-C(O)NR^9NR^9C(O)R^9$ ,
- (23)  $-(CH_2)_{0-1}-NR^9S(O)_{1-2}R^9$ ,
- (24)  $-(CH_2)_{0-1}-S(O)_{1-2}N(R^9)_2$ ,
- (25)  $-(CH_2)_{0-1}-S(O)_{0-2}R^9$ ,
- (26)  $O(CH_2)_{0-1}-C(O)N(R^9)_2$ ,
- (27) CF<sub>3</sub>,
- (28) CH<sub>2</sub>CF<sub>3</sub>,
- (29) OCF3, and
- (30) OCH<sub>2</sub>CF<sub>3</sub>,

wherein alkenyl, phenyl, naphthyl, heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, and wherein any alkyl, cycloalkyl, heterocycloalkyl, and methylene (CH<sub>2</sub>) carbon atom in  $R^3$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, oxo,  $C_{1-4}$  alkyl, trifluoromethyl, and  $C_{1-4}$  alkoxy, or two  $R^3$  substituents on the same carbon atom are taken together with the carbon atom to form a cyclopropyl group;

each  $R^4$  is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3)  $-(CH_2)_{0-1}-C_{3-6}$  cycloalkyl,
- (4)  $-(CH_2)_{0-1}$ -aryl,

- (5) hydroxy,
- (6) halogen, and
- (7) amino;

R<sup>5</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) C<sub>2-8</sub> alkenyl,
- (4) C<sub>2-8</sub> alkynyl,
- (5) C<sub>1-8</sub> alkoxy,
- (6)  $-(CH_2)_{0-1}-C_{3-7}$  cycloalkyl,
- (7)  $-(CH_2)_{0-1}-C_{2-7}$  heterocycloalkyl,
- (8)  $-(CH_2)_{0-1}$ -phenyl,
- (9)  $-(CH_2)_{0-1}$ -naphthyl,
- (10) -(CH<sub>2</sub>)<sub>0-1</sub>-heteroaryl, and
- (11) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>3</sub>-7 bicycloalkyl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from  $R^3$ , and alkyl, alkenyl, alkynyl, alkoxy, cycloalky, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from  $R^3$  and oxo, and wherein any methylene (CH<sub>2</sub>) in  $R^5$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl;

 $R^6$  is selected from the group consisting of

- (1) hydrogen, and
- (2) C<sub>1-8</sub> alkyl;

R<sup>7</sup> is selected from the group consisting of

- (1)  $-(CH_2)_{0-3}-N(R^8)_{2}$ ,
- (2)  $-(CH_2)_{0-3}-NR^8C(O)R^8$ ,
- (3)  $-(CH_2)_{0-3}-NR^8C(O)OR^8$ ,
- (4)  $-(CH_2)_{0-3}-NR^8C(O)N(R^8)_2$ ,
- (5)  $-(CH_2)_{0-3}-NR^8S(O)R^8$ ,
- (6)  $-(CH_2)_{0-3}-NR^8S(O)_2R^8$ , and
- (7)  $-(CH_2)_{0-3}-NR^8S(O)_2N(R^8)_2$ ,

wherein any methylene (CH<sub>2</sub>) in  $R^7$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl, or two  $R^8$  substituents together with the carbon, nitrogen or sulfur atom to which they are attached form a 5, 6, or 7-membered saturated or unsaturated nitrogen containing ring optionally substituted with one to three groups independently selected from  $C_{1-8}$  alkyl and oxo;

each R<sup>8</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2)  $C_{1-8}$  alkyl,
- (3) C<sub>2-8</sub> alkenyl,
- (4) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>3</sub>-7 cycloalkyl,
- (5) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>2-7</sub> heterocycloalkyl,
- (6) -(CH<sub>2</sub>)<sub>0-1</sub>-C<sub>3-7</sub> bicycloalkyl,
- (7)  $-(CH_2)_{0-1}$ -phenyl,
- (8) -(CH<sub>2</sub>)<sub>0-1</sub>-naphthyl, and
- (9)  $-(CH_2)_{0-1}$ -heteroaryl,

wherein alkyl, alkenyl, cycloalkyl, heterocycloalkyl, and bicycloalkyl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup> and oxo, and wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R<sup>3</sup>, and wherein any methylene (CH<sub>2</sub>) in R<sup>8</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1-4</sub> alkyl, or two R<sup>8</sup> groups together with the atom to which they are attached form a 5- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

each R<sup>9</sup> is independently selected from the group consisting of

- (1) hydrogen,
- (2) C<sub>1-8</sub> alkyl,
- (3) phenyl,
- (4) heteroaryl,
- (5) -(CH<sub>2</sub>)<sub>0-1</sub> heterocycloalkyl, and
- (6) C<sub>3</sub>-6 cycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C<sub>1-4</sub> alkyl, hydroxy, and C<sub>1-4</sub> alkoxy, or two

Page No.: 26

 $R^9$  groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC<sub>1-4</sub> alkyl;

r is 1 or 2;

0, 1 or 2; and s is

0, 1, 2, 3 or 4. m is

> The compound of Claim 1 selected from the group consisting of: 18. (original)

Serial No.: Case No.: Page No.: 10/788,859 21291Y

27

Me Me Me Me Me 0 Me Me Me Me Me Me 0 0 0 Me Me Me Me Me Me 0

or a pharmaceutically acceptable salt thereof.

19. (original) The compound of Claim 1 selected from the group consisting of:

Serial No.: 10/788,859 Case No.: Page No.: 21291Y

29

or a pharmaceutically acceptable salt thereof.

The compound of Claim 18 which is: 20. (original)

or a pharmaceutically acceptable salt thereof.

21. (original) The compound of Claim 18 which is:

or a pharmaceutically acceptable salt thereof.

## 22. (original) The compound of Claim 18 which is:

or a pharmaceutically acceptable salt thereof.

## 23. (original) The compound of Claim 18 which is:

or a pharmaceutically acceptable salt thereof.

## 24. (original) The compound of Claim 18 which is:

or a pharmaceutically acceptable salt thereof.

- 25. (original) A method for the treatment or prevention of disorders, diseases or conditions responsive to the activation of the melanocortin-4 receptor in a mammal in need thereof which comprises administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.
- 26. (original) A method for the treatment or prevention of obesity in a mammal in need thereof which comprises administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.
- 27. (original) A method for the treatment or prevention of diabetes mellitus in a mammal in need thereof comprising administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.
- 28. (original) A method for the treatment or prevention of male or female sexual dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.
- 29. (original) A method for the treatment or prevention of erectile dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.
- 30. (original) A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

31. (original) The pharmaceutical composition of Claim 30 further comprising a second active ingredient selected from the group consisting of an insulin sensitizer, an

insulin mimetic, a sulfonylurea, an α-glucosidase inhibitor, a HMG-CoA reductase inhibitor, a serotonergic agent, a β3-adrenoreceptor agonist, a neuropeptide Y1 antagonist, a neuropeptide Y5 antagonist, a pancreatic lipase inhibitor, a cannabinoid CB<sub>1</sub> receptor antagonist or inverse agonist, a

melanin-concentrating hormone receptor antagonist, a bombesin receptor subtype 3 agonist, and a ghrelin

receptor antagonist.

32. (original) The pharmaceutical composition of Claim 30 further comprising a second active ingredient selected from the group consisting of a type V cyclic-GMP-selective phosphodiesterase inhibitor, an α2-adrenergic receptor antagonist, and a dopaminergic agent.

33. (original) A method of treating erectile dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of the composition of Claim 30.

34. (original) A method of treating erectile dysfunction in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with a type V cyclic-GMP-selective phosphodiesterase inhibitor, an  $\alpha_2$ -adrenergic receptor antagonist, or a dopaminergic agent.

- 35. (original) A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of the composition of Claim 30.
- 36. (original) A method of treating obesity in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of the composition of Claim 30.
- 37. (original) A method of treating diabetes or obesity in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with an insulin sensitizer, an insulin mimetic, a sulfonylurea, an α-glucosidase inhibitor, a HMG-CoA reductase inhibitor, a serotonergic agent, a β3-adrenoreceptor agonist, a neuropeptide Y1 antagonist, a neuropeptide Y5 antagonist, a pancreatic lipase inhibitor, a cannabinoid CB<sub>1</sub> receptor antagonist or inverse agonist, a melanin-concentrating hormone receptor antagonist, a bombesin receptor subtype 3 agonist, or a ghrelin receptor antagonist.

38. (original) The compound of Claim 1 wherein the pharmaceutically acceptable salt thereof is the hydrochloride salt.

39. (original) The compound of Claim 1 wherein the pharmaceutically acceptable salt thereof is the trifluoroacetic acid salt.

40. (original) The compound of Claim 1 wherein the pharmaceutically acceptable salt thereof is the bis phosphate salt.

Claims 41 – 46 (cancelled)

47. (new) The compound of Claim 19 which is:

or a pharmaceutically acceptable salt thereof.

48. (new) The compound of Claim 19 which is:

or a pharmaceutically acceptable salt thereof.